Name of Policy:  
Bioimpedance Devices for Detection of Lymphedema

Policy #: 438  
Category: Medicine  
Latest Review Date: January 2016  
Policy Grade: C

Background/Definitions:
As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:
1. The technology must have final approval from the appropriate government regulatory bodies;
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;
3. The technology must improve the net health outcome;
4. The technology must be as beneficial as any established alternatives;
5. The improvement must be attainable outside the investigational setting.

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. In accordance with generally accepted standards of medical practice; and
2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient’s illness, injury or disease; and
3. Not primarily for the convenience of the patient, physician or other health care provider; and
4. Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient’s illness, injury or disease.
**Description of Procedure or Service:**
Secondary lymphedema may develop following surgery for breast cancer. Bioelectrical impedance is being studied as a diagnostic test for lymphedema, particularly for subclinical disease.

Secondary lymphedema of the upper extremity may develop following surgical treatment for breast cancer; it has been reported in about 25 to 50% of women following mastectomy. This can be a chronic, disfiguring condition. It results from lymphatic dysfunction or disruption, and can be difficult to accurately diagnose and manage. One challenge is identifying the presence of clinically significant limb swelling through simple noninvasive methods. Many techniques have been used for documenting lymphedema including differences in limb volume (volume displacement) and limb circumference measurements. A number of newer techniques are being evaluated, including bioimpedance with use of bioimpedance spectroscopy (BIS) analysis, which uses resistance to electrical current in comparing the composition of fluid compartments. BIS is based on the theory that the amount of opposition to flow of electric current (impedance) through the body is inversely proportional to the volume of fluid in the tissue. In lymphedema, with the accumulation of excess interstitial fluid, tissue impedance decreases.

The detection of subclinical lymphedema, that is, the early detection of lymphedema before clinical symptoms become apparent is another area of study. Detection of subclinical lymphedema (referred to as Stage 0 lymphedema) is problematic. Subclinical disease may exist for months or years before overt edema is noted. This approach generally involves comparison of preoperative with postoperative measurements, since existing differences between upper extremities (like the effects of a dominant extremity) may obscure early, subtle differences due to initial accumulation of fluid. Bioimpedance has been proposed as one diagnostic test for this condition. Those who support the approach to diagnose subclinical disease believe that early treatment of subclinical lymphedema should result in less severe chronic disease.

**Policy:**

**Devices using bioimpedance (bioelectrical impedance spectroscopy) do not meet** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage and are considered **investigational** for use in the diagnosis, surveillance, or treatment of patients with lymphedema, including use in subclinical secondary lymphedema.

*Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the member’s contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.*
Key Points:
Assessment of a diagnostic technology typically focuses on three parameters: 1) its technical performance; 2) diagnostic performance (sensitivity, specificity, and positive and negative predictive value) in appropriate populations of patients; and 3) demonstration that the diagnostic information can be used to improve patient outcomes (clinical utility). While in some cases, tests can be adequately evaluated using technical and diagnostic performance, when a test identifies a new or different group of patients with a disease, randomized controlled trials (RCTs) are needed to demonstrate impact of the test on the net health outcome.

When this policy was created, a literature review was conducted using MEDLINE through January 2010 to identify relevant studies. The review has been updated regularly with MEDLINE searches, most recently through November 21, 2015.

Technical Performance
Technical performance of a device is typically assessed with two types of studies, those that compare test measurements with a gold standard and those that compare results taken with the same device on different occasions (test-retest). While there is no absolute gold standard for diagnosis of lymphedema, the de facto gold standards are limb volume and/or limb circumference. Studies that address technical performance of bioimpedance devices are described next.

A 2010 publication by Czerniec and colleagues reported on measurement of lymphedema in a small group of patients, 33 with lymphedema and 18 without. This study was to determine the relationship between physical methods of measuring lymphedema and self-reported swelling. Measurement techniques included self-report, bioimpedance spectroscopy, perometer, and the truncated cone method. The authors noted that the physical measurement tools were highly reliable with high concordance (0.89 to 0.99, respectively). In this study, self-report correlated moderately with physical measurements (0.65 to 0.71, respectively) and was moderately reliable. The authors concluded that lymphedema assessment methods are concordant and reliable but not interchangeable.

In a U.S.-based study published in 2007, Warren and colleagues evaluated 15 patients with upper- or lower-extremity secondary lymphedema documented by lymphoscintigraphy, along with seven healthy controls using BIS analysis. In addition, both the affected and unaffected limbs in lymphedema patients were evaluated so patients also served as their own controls. According to BIS in the lymphedema patients, the average ratio of current flow of the affected limb to the unaffected limb (the impedance ratio) was 0.9 (range: 0.67 to 1.01). In the control group, the average impedance ratio was 0.99 (range: 0.95 to 1.02). Lower impedance ratio values correlated with higher levels of accumulated fluid.

Diagnostic Performance
A technology assessment on the diagnosis and treatment of secondary lymphedema, performed under contract from Agency for Healthcare Research and Quality (AHRQ) by the McMaster University Evidence-based Practice Center, was released in May 2010. As of October 2014, this assessment has not been updated. The assessment identified eight studies that reported the sensitivity and specificity of tests to diagnose secondary lymphedema. The investigators noted
that there is no true “gold standard” to grade severity of lymphedema and that limb volume and circumference are used as a de facto “gold standards.” Two of the 8 studies on diagnostic performance of devices to detect secondary lymphedema evaluated bioimpedance devices. Overall, the investigators concluded that, due largely to heterogeneity among studies, the evidence does not permit conclusions on the optimal diagnostic test for detection of secondary lymphedema.

Subsequent to the AHRQ review, several additional studies have been published on the diagnostic performance of bioimpedance devices for detecting lymphedema. Prospective studies that compared bioelectrical impedance analysis to a reference standard are described next.

A 2015 study by Barrio et al enrolled 223 women with newly diagnosed breast cancer and a plan for unilateral axillary surgery. Thirty-seven patients were excluded due to ineligibility or withdrawal, leaving a sample size of 186. Prior to surgery, participants received baseline volumetric measurements with a bioimpedance device (L-Dex) and volume displacement (VD, the reference standard). Patients then had regular follow-up volumetric measurements every three to six months for three years. At the last follow-up (median, 18.2 months), 152 patients (82%) were normal, 21 (11%) had an abnormal L-Dex and no lymphedema by VD, four (2%) had an abnormal L-Dex and lymphedema by VD and nine (5%) had lymphedema without prior L-Dex abnormality. In an analysis including only patients with at least six months of follow-up, L-Dex had a sensitivity of 31% (4/13) and a specificity of 88% (129/147) for predicting subsequent lymphedema development. In addition, the correlation between changes in VD and changes in L-Dex results were in the low to moderate range at three months ($r=0.31$) and six months ($r=0.21$). However, at the time of lymphedema diagnosis, the L-Dex ratio was abnormal in 12/13 patients (diagnostic sensitivity, 92%).

Another prospective study (published in 2015, by Blaney et al) included 126 women newly diagnosed with stages I-III unilateral breast cancer. A total of 115 women underwent baseline assessment with a bioimpedance device (L-Dex) and circumferential measurement (CM). CM was used as the reference standard, although the authors note the test is an imperfect “gold standard”. Postsurgical follow-up assessments were planned every six months for a year. The number of women completing these assessments was 109 (95%) at three months, 89 (77%) at six months, 79 (69%) at nine months and 71 (62%) at 12 months. During the 12-month study, 31 participants were identified as having lymphedema by at least one of the assessment methods. Twenty-eight of 31 (90%) were identified by CM and 11 (35%) by bioimpedance analysis. There was no statistically significant correlation between bioimpedance analysis and CM.

Section Summary: Diagnostic Performance
An AHRQ technology assessment published in 2010 identified few studies on bioimpedance analysis for diagnosing lymphedema. A few prospective studies have been published subsequent to the AHRQ review, and these tended to find suboptimal correlation between bioimpedance analysis and the reference standard. In the one study that reported measures of diagnostic accuracy, bioimpedance analysis had a low sensitivity and specificity for predicting lymphedema development.
Clinical Utility
The ideal study design is an RCT comparing health outcome in patients who were managed with and without the use of bioimpedance devices. No RCTs were identified. However, there was one controlled observational study comparing clinical lymphedema rates in patients managed with and without bioimpedance analysis. This study, published by Soran et al in 2014, involved prospective detection of subclinical lymphedema in 186 women with breast cancer who were managed with L-Dex or tape measurement of limb circumference. Measurements were obtained at baseline and at three to six-month intervals for five years. Subclinical lymphedema was defined as an L-Dex value outside the normal range or that increased at least 10 units from baseline. Patients diagnosed with subclinical lymphedema were treated with short-term physical therapy, compression garments and received education on exercise, limb elevation, etc. A total of 180 women were included in the analysis. Seventy-two women had both preoperative and postoperative bioimpedance and tape measurements (“preoperative group”). Forty-four women had preoperative bioimpedance and tape measurements but only had tape measurements postoperatively (“control group”). The remaining 64 women had postoperative bioimpedance and tape measurements, but no preoperative measurements (“no preoperative group”). The authors compared demographic and clinical characteristics in the preoperative and control groups, and in the preoperative and postoperative groups and did not identify any statistically significant differences.

In the preoperative group, 28 of 72 women (36%) were diagnosed with subclinical lymphedema and referred for treatment; two women progressed to clinical lymphedema. In the control group, 16 women (36%) developed clinical lymphedema during follow-up. A limitation of the study is that there was no alternative method for detecting subclinical women in the control group so that they could receive treatment early. Moreover, the women were not randomized to a treatment group and complete information (pre- and postoperative measures of lymphedema) was available for only a subset of the total population.

Section Summary: Clinical Utility
One prospective comparative study was identified that compared rates of clinical lymphedema in women managed with and without bioimpedance analysis. This study had several limitations, including nonrandomized design, lack of blinding lack of complete information on a substantial number of patients in the study, and lack of a systematic method for diagnosing lymphedema in the control group. The authors reported a significantly lower rate of clinical lymphedema in patients who were managed with bioimpedance analysis and who received treatment for subclinical lymphedema. Additional studies to confirm these findings are needed, especially RCTs and those that include an alternative method for early or subclinical lymphedema detection.

Summary of Evidence
The evidence on bioimpedance devices in individuals with known or suspected lymphedema includes several prospective studies on diagnostic accuracy and a controlled observational study evaluating clinical utility. Relevant outcomes are test accuracy and validity, symptoms, and quality of life. Recent diagnostic accuracy studies found a poor correlation between bioimpedance analysis and the reference standard (volume displacement or circumferential measurement). There were no randomized controlled trials (RCTs) evaluating the clinical utility of bioimpedance devices in the management of patients with lymphedema or at high risk of

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developing lymphedema. The single prospective comparative study found a significantly lower rate of clinical lymphedema in patients managed with bioimpedance devices. Limitations of this study include the retrospective design, lack of randomized or blinding, and lack of a systematic method of detecting early or subclinical lymphedema in the control group. The evidence is insufficient to determine the effects of the technology on health outcomes.

Practice Guidelines and Position Statements
No relevant practice guidelines or position statements were identified.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Key Words:
Bioelectrical impedance testing, Bioimpedance spectroscopy, Lymphedema, bioimpedance testing, Bioimpedance analysis, BIS, Impedance plethysmography, Impedimed, LDex, Plethysmography

Approved by Governing Bodies:
In 2007, the ImpediMed L-Dex™ U400 was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process as an aid in the clinical assessment of unilateral lymphedema of the arm in women. It is not intended to diagnose or predict lymphedema.

Benefit Application:
Coverage is subject to member’s specific benefits. Group specific policy will supersede this policy when applicable.

ITS: Home Policy provisions apply
FEP: Special benefit consideration may apply. Refer to member’s benefit plan. FEP does not consider investigational if FDA approved and will be reviewed for medical necessity.

Current Coding:
CPT Codes: 93702 Bioimpedance spectroscopy (BIS), extracellular fluid analysis for lymphedema assessment(s) (Effective January 1, 2015)

Previous Coding:
0239T Bioimpedance spectroscopy (BIS), measuring 100 frequencies or greater, direct measurement of extracellular fluid differences between the limbs (Deleted January 1, 2015)
References:


Policy History:
Medical Policy Group, June 2010 (3)
Medical Policy Administration Committee, July 2010
Available for comment July 2-August 16, 2010
Medical Policy Group, December 2010 – Added Code effective Jan 1, 2011
Medical Policy Group, April 2011: Added 2011 Update-Key Points, Updated References
Medical Policy Group, September 2012 (3): 2012 Update to Key Points & References
Medical Policy Group, November 2012 (3): Additional 2012 Updates to Key Points and References
Medical Policy Panel, November 2013
Medical Policy Group, November 2013 (3): Updated Key Points and References; no change in policy statement
Medical Policy Panel, January 2016
Medical Policy Group, January 2016 (6): Updates to Key Points, Approved by Governing Bodies and References; no change to policy statement.

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member’s plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield’s administration of plan contracts.